Appl. No. 10/028,989

Amdt. dated February 26, 2009

Reply to Office Action of November 26, 2008

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-68. (canceled)

- 69. (currently amended): A method of delivering a <u>drug substance</u> into an intradermal compartment of a human subject's skin, said method comprising administering the <u>drug substance</u> through at least one small gauge hollow needle having an outlet with an exposed height between 0 and 1 mm, said outlet being inserted into the skin to a depth of between 0.3 mm and 2 mm, such that delivery of the <u>drug substance</u> occurs at a depth between 0.3 mm and 2 mm, wherein a dosage of the <u>drug substance</u> for achieving a systemic bioavailability of the <u>drug substance</u> is reduced by at least 10% compared to the dose required to achieve the systemic bioavailability when the <u>drug substance</u> is delivered to a subcutaneous compartment of the human subject's skin, wherein the systemic bioavailability of the drug is measured by a determination of its AUC.
- 70. (previously presented): The method of claim 69, wherein the systemic bioavailability results in a therapeutic or diagnostic effect.
- 71. (currently amended): The method of claim 69 wherein the administering comprises inserting the needle so that the <u>drug substance</u> is deposited at a depth of at least about 0.3 mm below the surface of the human subject's skin to no more than about 2 mm below the surface of the human subject's skin.
- 72. (currently amended): The method of claim 69 wherein the administering comprises inserting the needle into the skin so that the <u>drug substance</u> is deposited at a depth of at least about 0.3 mm and no more than about 2 mm.
- 73. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is administered over a time period of not more than ten minutes.

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- 74. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is administered at a rate between 1 nL/min and 200 mL/ min.
- 75. (previously presented): The method of claim 69 wherein the needle(s) are inserted substantially perpendicularly to the skin.
- 76. (canceled)
- 77. (previously presented): The method of claim 69 wherein the dosage is reduced by at least 20%.
- 78. (previously presented): The method of claim 69 wherein the dosage is reduced by at least 30%.
- 79. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is a peptide, protein or nucleic acid.
- 80. (canceled)
- 81. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is hydrophobic.
- 82. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is hydrophilic.
- 83. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is a hormone.
- 84. (currently amended): The method of claim 69 wherein the <u>drug substance</u> is selected from the group consisting of insulin, granulocyte stimulating factor and PTH.

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85. (currently amended): A method of delivering a <u>drug substance</u> into an intradermal compartment of a human subject's skin, said method comprising injecting or infusing the <u>drug substance</u> intradermally through one or more microneedles having a length sufficient to penetrate the intradermal compartment and an outlet at a depth within the intradermal compartment wherein a dosage of the <u>drug substance</u> for achieving a systemic bioavailability of the <u>drug substance</u> is reduced by at least 10% compared to the dose required to achieve the systemic bioavailability when the <u>drug substance</u> is delivered to a subcutaneous compartment of the human subject's skin, <u>wherein the systemic bioavailability of the drug is measured by a determination of its AUC</u>.

- 86. (previously presented): The method of claim 85 wherein the length of the microneedle(s) is from about 0.5 mm to about 1.7 mm.
- 87. (previously presented): The method of claim 85 wherein the microneedle is a 30 to 34 gauge needle.
- 88. (previously presented): The method of claim 85 wherein the microneedle has an outlet with an exposed height between 0 and 1 mm.
- 89. (previously presented): The method of claim 85 wherein the microneedle is configured in a delivery device which positions the microneedle perpendicular to skin surface.
- 90. (previously presented): The method of claim 85 wherein the microneedle is contained in an array of microneedles.
- 91. (previously presented): The method of claim 90 wherein the array comprises 3 microneedles.
- 92. (previously presented): The method of claim 90 wherein the array comprises 6 microneedles.

- 93. (currently amended): The method of claim 85 wherein the <u>drug</u> substance is administered over a time period of not more than ten minutes.
- 94. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is administered at a rate between 1 nL/min and 200 mL/min.
- 95. (previously presented): The method of claim 85 wherein the microneedle(s) are inserted substantially perpendicularly to the skin.
- 96. (canceled)
- 97. (previously presented): The method of claim 85 wherein the dosage is reduced by at least 20%.
- 98. (previously presented): The method of claim 85 wherein the dosage is reduced by at least 30%.
- 99. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is a peptide, protein, or nucleic acid.
- 100. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is a hormone.
- 101. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is hydrophobic.
- 102. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is hydrophilic.
- 103. (currently amended): The method of claim 85 wherein the <u>drug substance</u> is selected from the group consisting of insulin, granulocyte stimulating factor and PTH.

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104. (currently amended): The method of claim 69 or 85 wherein the <u>drug substance</u> is used for the treatment of a symptom of a pathological condition.

105. (currently amended): The method of claim 85, wherein delivery of the <u>drug</u> substance occurs at a depth between 0.3 to 2.0 mm

Claims 106-107 (canceled)